

CLAIMS

What we claim is:

1. A double-stranded short interfering nucleic acid (siNA) molecule comprising about 19 to about 21 base pairs, wherein said siNA comprises nucleotide sequence complementary to nucleic acid sequence encoding vascular endothelial growth factor receptor 1 (VEGFr1) and vascular endothelial growth factor receptor 2 (VEGFr2) or a portion thereof, and wherein said siNA down-regulates either VEGFr1 or VEGFr2 gene expression or both VEGFr1 and VEGFr2 gene expression.
2. The siNA molecule of claim 1, wherein said siNA molecule comprises no ribonucleotides.
3. The siNA molecule of claim 1, wherein said siNA molecule comprises ribonucleotides.
4. The siNA molecule of claim 1, wherein one of the strands of said double-stranded siNA molecule comprises a nucleotide sequence that is complementary to a nucleotide sequence present in both VEGFr1 and VEGFR2 encoded RNAs or a portion thereof, and wherein the second strand of said double-stranded siNA molecule comprises a nucleotide sequence substantially similar to the nucleotide sequence of said VEGFr1 and VEGFR2 encoded RNAs or a portion thereof.
5. The siNA molecule of claim 4, wherein each said strand of the siNA molecule comprises about 19 to about 23 nucleotides, and wherein each said strand comprises at least about 19 nucleotides that are complementary to the nucleotides of the other strand.
6. The siNA molecule of claim 1, wherein said siNA molecule comprises an antisense region and a sense region, wherein said antisense region comprises a nucleotide sequence that is complementary to a nucleotide sequence present in both VEGFr1 and VEGFR2 encoded RNAs or a portion thereof, and wherein said sense region comprises a nucleotide sequence substantially similar to the nucleotide sequence present in both VEGFr1 and VEGFR2 encoded RNAs or a portion thereof.
7. The siNA molecule of claim 6, wherein said antisense region and said sense region each comprise about 19 to about 23 nucleotides, and wherein said antisense region comprises at least about 19 nucleotides that are complementary to nucleotides of the sense region.

8. The siNA molecule of claim 1, wherein said siNA molecule comprises a sense region and an antisense region and wherein said antisense region comprises a nucleotide sequence that is complementary to a nucleotide sequence or a portion thereof of RNA encoded by a VEGFr1 and VEGFR2 gene and said sense region comprises a nucleotide sequence that is complementary to said antisense region.
9. The siNA molecule of claim 6, wherein said siNA molecule is assembled from two separate oligonucleotide fragments wherein one fragment comprises the sense region and the second fragment comprises the antisense region of said siNA molecule.
10. The siNA molecule of claim claim 6, wherein said sense region is connected to the antisense region via a linker molecule.
11. The siNA molecule of claim 10, wherein said linker molecule is a polynucleotide linker.
12. The siNA molecule of claim 10, wherein said linker molecule is a non-nucleotide linker.
13. The siNA molecule of claim 6, wherein pyrimidine nucleotides in the sense region are 2'-O-methyl pyrimidine nucleotides.
14. The siNA molecule of claim 6, wherein purine nucleotides in the sense region are 2'-deoxy purine nucleotides.
15. The siNA molecule of claim 6, wherein the pyrimidine nucleotides present in the sense region are 2'-deoxy-2'-fluoro pyrimidine nucleotides.
16. The siNA molecule of claim 9, wherein the fragment comprising said sense region includes a terminal cap moiety at the 5'-end, the 3'-end, or both of the 5' and 3' ends of the fragment comprising said sense region.
17. The siNA molecule of claim 16, wherein said terminal cap moiety is an inverted deoxy abasic moiety.
18. The siNA molecule of claim 6, wherein the pyrimidine nucleotides of said antisense region are 2'-deoxy-2'-fluoro pyrimidine nucleotides
19. The siNA molecule of claim 6, wherein the purine nucleotides of said antisense region are 2'-O-methyl purine nucleotides.

20. The siNA molecule of claim 6, wherein the purine nucleotides present in said antisense region comprise 2'-deoxy- purine nucleotides.
21. The siNA molecule of claim 18, wherein said antisense region comprises a phosphorothioate internucleotide linkage at the 3' end of said antisense region.
- 5 22. The siNA molecule of claim 6, wherein said antisense region comprises a terminal cap moiety at the 3' end of said antisense region.
23. The siNA molecule of claim 22, wherein said terminal cap comprises an inverted deoxyabasic moiety.
- 10 24. The siNA molecule of claim 22, wherein said terminal cap comprises a glyceryl moiety.
25. The siNA molecule of claim 9, wherein each of the two fragments of said siNA molecule comprise 21 nucleotides.
- 15 26. The siNA molecule of claim 25, wherein about 19 nucleotides of each fragment of the siNA molecule are base-paired to the complementary nucleotides of the other fragment of the siNA molecule and wherein at least two 3' terminal nucleotides of each fragment of the siNA molecule are not base-paired to the nucleotides of the other fragment of the siNA molecule.
27. The siNA molecule of claim 26, wherein each of the two 3' terminal nucleotides of each fragment of the siNA molecule are 2'-deoxy-pyrimidines.
- 20 28. The siNA molecule of claim 27, wherein said 2'-deoxy-pyrimidine is 2'-deoxy-thymidine.
29. The siNA molecule of claim 25, wherein all 21 nucleotides of each fragment of the siNA molecule are base-paired to the complementary nucleotides of the other fragment of the siNA molecule.
- 25 30. The siNA molecule of claim 25, wherein about 19 nucleotides of the antisense region are base-paired to the nucleotide sequence of the RNA encoded by a VEGFr1 and VEGFr2 gene or a portion thereof.
- 30 31. The siNA molecule of claim 25, wherein 21 nucleotides of the antisense region are base-paired to the nucleotide sequence of the RNA encoded by a VEGFr1 and VEGFr2 gene or a portion thereof.

32. The siNA molecule of claim 9, wherein the 5'-end of the fragment comprising said antisense region optionally includes a phosphate group.
33. A double-stranded short interfering nucleic acid (siNA) molecule that inhibits the expression of a VEGFr1 and a VEGFr2 gene, wherein said siNA molecule comprises
5 no ribonucleotides and wherein each strand of said double-stranded siNA molecule comprises about 21 nucleotides.
34. A double-stranded short interfering nucleic acid (siNA) molecule that inhibits the expression of a VEGFr1 and a VEGFr2 gene, wherein said siNA molecule does not
10 require the presence of a ribonucleotide within the siNA molecule for inhibition of VEGFr1 and VEGFr2 gene expression and wherein each strand of said double-stranded siNA molecule comprises about 21 nucleotides.
35. A pharmaceutical composition comprising the siNA molecule of claim 1 in an acceptable carrier or diluent.